STUDY

Contact Allergy in Children Referred for Patch Testing

North American Contact Dermatitis Group Data, 2001-2004

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Objectives: To determine the frequency of positive and relevant patch tests in children referred for patch testing in North America; to compare results of patch testing children and adults; and to compare our results with international data on contact allergy in children.

Design: Retrospective cross-sectional analyses of North American Contact Dermatitis Group (NACDG) data from January 1, 2001, through December 31, 2004. Patch test reactions for allergens that were positive and considered of clinical importance to the patient's eczematous problem were defined as being of current or past relevance.

Setting: Clinical patch test data from 13 NACDG members, primarily a referral population.

Patients: The pediatric population (hereafter referred to as "children") was defined as patients aged 0 to 18 years (n=391). Patients 19 years and older constituted the comparison adult group (n=9670).

Main Outcome Measures: The frequency of positive patch test reactions and number of relevant ones. Secondary measures included the association of atopic markers, frequency of irritant reactions, and sources of relevant supplementary allergens.

Results: No significant difference in the overall frequency of at least 1 relevant positive patch test reaction was noted in children (51.2%) compared with adults (54.1%). The most frequent positive reactions in children were to nickel (28.3%), cobalt chloride (17.9%), thimerosal (15.3%), neomycin sulfate (8.0%), gold sodium thiosulfate (7.7%), and fragrance mix (5.1%). For children aged 0 to 18 the most frequent relevant positive reactions were to nickel sulfate (26.0%), cobalt (12.4%), neomycin (4.4%), fragrance mix (4.1%), gold (3.6%), and quaternium 15 (3.6%). The frequency of irritant reactions in adults and children was similar. Of the children with a relevant positive reaction, 34.0% had atopic dermatitis included as one of their final diagnoses, compared with 11.2% of adults ($P<.001$). Fifteen percent and 39% of children had relevant allergens not included in the NACDG series and a commercially available skin patch test (T.R.U.E. TEST [thin-layer rapid use epicutaneous test], panel 1.1 and 2.1; Allerderm, Phoenix, Arizona), respectively.

Conclusions: Adults and children in this group are equally likely to have allergic contact dermatitis; frequency of relevant allergen reactions differs.

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ECZEMATOUS DERMATITIS, including atopic dermatitis and contact dermatitis, is common in children. In 1999, Mortz and Andersen[1] reviewed 17 studies on patch testing in children. They reported that, overall, 14.5% to 70.7% of children suspected of having contact dermatitis had positive patch test reactions. As shown in **Table 1**, all of those studies were from outside North America, most were from a single center, and only some reported clinical relevance, which is essential for interpretation and effective clinical management.

The purpose of this study was to examine the frequency and relevance of positive reactions for allergens in children referred for patch testing, and to compare these results with those of our adult population undergoing patch testing. We compared our results with recent international data on pediatric patch testing and explored differences in results by sex and by stratified age ranges. We examined the frequency of irritant reactions in this age group compared with adults and determined which allergens were most frequently responsible for irritant patch test reactions in the pediatric population. We examined the frequency and type of allergens not part of the routine North American Contact Dermatitis Group (NACDG) screening series but yielding relevant re-

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Table 1. Recent Retrospective Analyses of Patch Tested Children With Suspected ACD

Source (No. of Centers)/ Country	Data Collection, Years	No. of Children in Study	Age, y	Children With >1 Positive Reaction, %	Relevance	Most Common Allergens (Frequency of Positive Reactions)
Beattie et al,[2] 2007 (single center)/United Kingdom	1999-2002	114	3-15	54	54%[a]	Nickel (20%) Rubber chemicals (10%) Fragrance (7.2%) Cobalt (5.4%) Lanolin (4.5%)
Clayton et al,[3] 2006 (single center)/United Kingdom	1995-2004	500	0-16	27	61% of Reactions of current clinical relevance	Nickel (33%) Fragrance mix (18%) Cobalt (11%) Mercapto chemicals (8%) Balsam of Peru (*Myroxylon pereirae*) (8%)
Fernández Vozmediano and Armario Hita,[4] 2005 (single center)/Spain	1990-2000	96	≤15	52	8/18 8/16 13/15 3/6 2/4 1/4	Thimerosal (21%) Mercury (19%) Nickel (18%) Cobalt (6/96) Thiuram mix (4/96) Colophony (4/96)
Heine et al,[5] 2004 (multicenter)/ Germany, Austria, and Switzerland	1995-2002	2460	≤18	52.6 Children; 49.7 adolescents	[b]	Thimerosal (18.2%[c]; 14.3%[d]) Benzoyl peroxide (16.5%[c]; 8.0%[d]) Phenylmercuric acetate (13.1%[d]; 7.1%[c]) Gentamicin sulfate (12.5%[d]; 2.9%[c]) Nickel sulfate (10.3%[d]; 5.2%[c]) Ammoniated mercury (8.3%[d]; 5.2%[c])
Wöhrl et al,[6] 2003 (single center)/ Austria	1997-2000	79	1-10	62	Not reported	Nickel sulfate (34.2%) Ethyl mercury (35.3%) Thimerosal (17.7%) Copper sulfate (15.2%) Fragrance mix (12.7%)
Duarte et al,[7] 2003 (single center)/Brazil	1996-2001	102	10-19	56	All reported as clinically relevant	Nickel sulfate (31%) Tosylamide/formaldehyde resin (12%) Thimerosal (10%) Cobalt chloride (9%) Balsam of Peru (5%)
Roul et al,[8] 1999 (single center), France	1995-1997	337	1-15	66	Rare clinical correlation for nickel Most cases of fragrance relevant (9/11) Positive reaction to rubber allergen relevant	Nickel (24%) Fragrances (9%) Rubber chemicals (3%)

Abbreviation: ACD, allergic contact dermatitis.
[a] Relevance defined as current or present.
[b] Relevance not specifically identified by allergen.
[c] Adolescents (aged 13-18 years).
[d] Children (aged 6-12 years).

sults. We also compared the NACDG screening series results with potential results from testing with a currently available allergen screening series (T.R.U.E. TEST [thin-layer rapid use epicutaneous test], panels 1.1 and 2.1; Allerderm, Phoenix, Arizona).

METHODS

POPULATION, DATA COLLECTION, AND DETERMINATION OF ALLERGIC CONTACT DERMATITIS IN CHILDREN

The data collection project of the NACDG was deidentified, compliant with the Health Insurance Portability and Accountability Act, and designated as institutional review board exempt (Dartmouth-Hitchcock Medical Center committee for the protection of human subjects [CPHS 16236]). From January 1, 2001, through December 31, 2004, 13 NACDG members (2 Canadian and 11 American) conducted patch testing to a standard series of allergens (Chemotechnique Diagnostics AB, Malmö, Sweden) in 10 061 patients using Finn chambers (Epitest Ltd Oy, Tuusula, Finland) on a hypoallergenic plaster tape (Scanpor tape; Norgesplaster Alpharma AS, Vennesla, Norway) as previously described.[9] The interpretation of patch test reactions was standardized as previously reported.[9] A screening series of 65 allergens was tested with the addition of supplemental allergens deemed potentially relevant by the individual clinician. This screening series did not differ between children and adults. On occasion, some allergens were excluded from the test series owing to individual considerations, which may have included a previous known positive reaction to an allergen. From the 2001-2002 series to the 2003-2004 series, 6 allergens differed, resulting in a total of 71 al-

lergens in the 4-year period. At the time of patch test completion, clinical relevance of a positive reaction to an allergen test was determined by the investigator. Definitions of current relevance included definite (meaning a patch and/or use test with the suspected source yielded a positive reaction, or a patch test of the item or product yielded a positive reaction), probable (meaning the allergen could be verified as present in a known contactant of the patient), and possible (meaning the patient was exposed to circumstances in which skin contact with materials likely to contain the allergen was possible). Past relevance of a positive reaction to an allergen test could be indicated. For the purpose of this study, relevance data were combined to include present (definite, probable, and possible) and past relevance. Percentage of relevance in this study was defined as the number of relevant positive patch tests reactions (RPPTs) divided by the number of patients undergoing testing to a specific allergen. Final patch test interpretation codes included allergic, negative, or irritant.

For each currently relevant positive reaction to an allergen, a 3-digit code was used to indicate the suspect allergen source. As many as 3 final diagnoses, designated as *dermatitis type code*, were selected based on history, skin examination, and patch test results. Options included allergic contact dermatitis (ACD), irritant contact dermatitis, atopic dermatitis, stasis dermatitis, nummular dermatitis, other types of dermatitis, psoriasis or other noneczematous dermatoses, seborrheic dermatitis, or pompholyx.

Relevant allergen sources for supplemental allergens not included on the standard tray were noted when applicable. Whether the source was a specific allergen or a patient's personal product was not indicated. One positive relevant supplemental allergen only could be recorded. The supplemental allergen could include a product supplied by the patient, a chemical allergen, or other suspected item (eg, a shoe piece, an athletic pad).

A history of hay fever, atopic eczema, or asthma was recorded. Atopic predisposition was defined as having a history of at least 1 of the 3. The history of atopic eczema was determined by the experienced judgment of the individual NACDG investigator (all of the authors except D.M.-S.) and not stringent methods.

As of August 2007 in the United States, there were 23 commercially available T.R.U.E. TEST allergen patches. We determined an allergen on the NACDG series to be present in the T.R.U.E. TEST if it was listed as a component of a mixture or as an individual allergen. For hypothetical yields with the 23 T.R.U.E. TEST allergens, we used a similar method to that of Saripalli et al.[10] Briefly, a positive, currently relevant reaction to a component of a mix or an allergen present on the T.R.U.E. TEST was included and reported as the percentage of patients who would have had all their positive allergens detected using the T.R.U.E. TEST panels 1.1 and 2.1 only for testing. In addition, we also calculated the proportion of patients who had reactions to non-NACDG supplemental allergens.

ANALYTICAL METHODS

Data were manually entered into a centralized database (Access 2003; Microsoft Corporation, Redmond, Washington). Analyses were performed using commercially available statistical software (SPSS version 14; SPSS Inc, Chicago, Illinois) for this analysis. From the data set of 10 061 records, the pediatric study subset was defined as patients 18 years or younger undergoing patch testing (hereafter referred to as "children"). The adults 19 years and older constituted the comparison adult population.

Counts and proportions were determined to examine demographic and patch test data. Categorical (nominal) frequency data were statistically compared using χ^2 tests with $\alpha = .05$.

Table 2. Frequency of Atopic Markers in the Study Groups

Atopic Marker	Children (Aged 0-18 Years), % (n=391)	Adults (Aged ≥19 Years), % (n=9670)	Comparison Between Groups, *P* Value
Hay fever (allergic rhinitis)	24.0	26.0	>.3
Eczema	40.2	17.2	<.001
Asthma	21.5	13.1	<.001
Any	56.8	38	<.001

Table 3. Frequency of 1 or More Positive and Relevant Patch Test Reactions in Children and Adults

	Frequency, No. (%)	
	≥1 Positive Patch Test Reaction	≥1 Relevant Positive Patch Test Reaction
Children (n=391)	257 (65.7)	200 (51.2)
Adults (n=9670)	6564 (67.9)	5232 (54.1)

RESULTS

DEMOGRAPHICS

Ten thousand sixty-one patients underwent patch testing by the NACDG from January 1, 2001, through December 31, 2004. Of these, 391 patients were 18 years or younger. Fifteen were aged 0 to 5 years; 129, 6 to 12 years; and 247, 13 to 18 years. Two hundred fifty-four of 391 were female; 137 were male. The comparison adult group consisted of 9670 patients. No statistically significant difference was noted in the proportion of male and female patients in the pediatric vs the adult groups ($P > .70$). The racial composition of the pediatric group included white (n=337), black (n=25), Hispanic (n=14), Asian (n=12), and other (n=3) categories and was not statistically significantly different from the racial composition of the adult group. Atopic history markers were statistically higher in the pediatric population compared with the adult population except for hay fever (**Table 2**).

FREQUENCY OF POSITIVE ALLERGEN REACTION

The frequency of a diagnosis of contact allergy in the pediatric group as 1 of 3 possible final diagnoses was 200 of 391 (51.2%). This was not significantly different from the NACDG adult population (5232 of 9670 [54.1%]; $P > .25$).

The frequency of at least 1 RPPT in children and adults was similar (**Table 3**). Specific allergen frequencies for the pediatric and adult populations are listed in **Table 4**. Overall, frequencies were similar. Allergens that were statistically more frequent in children included nickel ($P < .001$), cobalt chloride ($P < .001$), and thimerosal

Table 4. Frequency of Positive Patch Test Reactions and Relevant Positive Reactions to Each Allergen[a]

Allergen	Children Aged 0-5 Years (n=15)		Children Aged 0-18 Years (n=391)		Adults Aged ≥19 Years (n=9670)	
	Positive, %	Relevant, %	Positive, %	Relevant, %	Positive, %	Relevant, %
Nickel sulfate, 2.5% pet	26.7	20.0	28.3	26.0	17.2	14.3
Cobalt chloride, 1% pet	14.3	7.1	17.8	12.4	7.5	5.0
Thimerosol, 0.1% pet[b]	25.0	0	15.4	2.1	10.0	3.5
Neomycin sulfate, 20% pet	13.3	13.3	8.0	4.4	11.2	7.9
Gold sodium thiosulfate, 0.5% pet	14.3	0	7.8	3.6	9.5	4.4
Fragrance mix, 8% pet	7.7	0	5.1	4.1	9.9	8.7
Myroxylon pereirae (balsam of Peru), 25% pet	0	0	3.9	2.3	11.4	9.5
Quaternium 15, 2% pet	7.1	7.1	3.6	3.6	9.3	8.3
Lanolin alcohol, 30% pet	0	0	3.6	2.8	2.1	1.9
Potassium dichromate, 0.25% pet	0	0	3.6	2.1	4.3	2.5
Colophony, 20% pet	0	0	3.3	2.8	2.7	1.9
Bacitracin, 20% pet	14.3	14.3	3.3	2.6	8.1	6.2
Propylene glycol, 30% aq	0	0	3.3	3.1	3.7	3.3
Formaldehyde, 1% aq	6.7	0	3.3	1.8	8.8	6.8
Benzalkonium chloride, 0.1% aq[b]	0	0	3.1	0.5	4.4	1.6
p-Phenylenediamine, 1% pet	0	0	2.3	2.1	4.9	3.6
Disperse blue dye 106, 1% pet	0	0	2.1	1.0	2.4	1.6
Diazolidinyl urea, 1% aq	0	0	2.1	2.1	2.9	2.6
Diazolidinyl urea, 1% pet	0	0	1.8	1.8	3.3	3.0
Mercaptobenzothiazole, 1% pet	0	0	1.8	1.8	1.1	1.0
Carba mix, 3% pet	0	0	1.8	1.5	4.5	3.9
Thiuram mix, 1% pet	0	0	1.8	1.3	4.7	4.2
Budesonide, 0.01% pet[c]	0	0	1.6	0.5	1.6	1.5
Compositae mix, 6% pet	0	0	1.6	0.5	1.2	0.9
Amidoamine, 0.1% pet	0	0	1.6	1.0	2.0	1.7
Cocamidopropyl betaine, 1% aq	0	0	1.6	0.8	2.3	2.1
2-Bromo-2-nitropropane-1,3-diol, 0.5% pet	0	0	1.5	1.3	2.9	2.1
Ethylenediamine dihydrochloride, 1.0% pet	0	0	1.5	0.8	2.6	1.4
di-Alpha tocopherol, 100%	0	0	1.3	0.8	1.1	0.9
Imidazolidinyl urea, 1% pet	0	0	1.3	1.3	3.0	2.8
Methylchoroisothiazolinone/methylisothiazolinone, 100 ppm aq	0	0	1.3	1.3	2.3	2.0
Ethyleneurea melamine-formaldehyde, 5% pet	0	0	1.3	1.0	2.2	1.5
p-tert-Butylphenol formaldehyde resin, 1% pet	0	0	1.3	1.3	1.9	1.1
Tea tree oil, oxidized, 5% pet[c]	14.3	14.3	1.1	1.1	0.9	0.6
Clobetasol 17-propionate, 1% pet[c]	0	0	1.0	1.6	0.7	0.6
Mixed dialkyl thioureas, 1% pet	0	0	1.0	0.8	0.9	0.7
Budesonide, 0.1% pet	0	0	1.0	1.0	1.4	1.3
Jasmine absolute oil, 2% pet	0	0	1.0	0.8	0.7	0.7
Mercapto mix, 1% pet	0	0	1.0	1.0	0.8	0.7
Tetracaine, 1% pet	0	0	0.8	0.3	0.4	0.1
Ylang-ylang oil, 2% pet	0	0	0.8	0.5	1.2	1.0
Iodopropynyl butylcarbamate, 0.1% pet	7.7	7.7	0.8	0.8	0.4	0.3
1,3-Dimethylol-5,5-dimethyl hydantoin, 1% aq	0	0	0.8	0.8	1.8	1.7
Tosylamide formaldehyde resin, 10% pet	0	0	0.8	0.5	1.6	1.3

(continued)

($P<.01$), whereas those that were significantly less frequent in the pediatric compared with the adult populations included neomycin sulfate ($P<.05$), fragrance mix ($P<.002$), balsam of Peru (*Myroxylon pereirae*) ($P<.001$), and quaternium 15 ($P<.001$).

The most frequent allergens in children were not necessarily the most relevant (**Table 5**). For example, 15.4% of the pediatric group had a positive reaction to thimerosal, but this allergen was not included in the top 10 relevant allergens.

PEDIATRIC SUBGROUPS BY AGE

Children aged 0 to 5 years underwent an average of 56.4 patch tests, whereas those aged 6 to 18 years underwent on average the full 65-allergen test series. Of the 15 patients in the very young group (<5 years), nickel was the allergen with the most frequent and relevant positive reactions. The only allergen that yielded positive reactions more frequently in any one of these age subsets was lanolin, which more commonly yielded positive reactions in children aged 6 to 12 years ($P<.01$).

ATOPIC DERMATITIS AS 1 OF THE 3 FINAL DIAGNOSES AND RPPTs

Most children with at least 1 RPPT also had a reported history of atopic eczema (19.95%), compared with adults (10.4%). Among the children with an RPPT, 34.0% had atopic dermatitis included as 1 of their final diagnoses, compared with 11.2% of adults with at least 1 RPPT ($P<.001$). Children with at least 1 of the 3 final diag-

Table 4. Frequency of Positive Patch Test Reactions and Relevant Positive Reactions to Each Allergen[a] (cont)

Allergen	Children Aged 0-5 Years (n=15)		Children Aged 0-18 Years (n=391)		Adults Aged ≥19 Years (n=9670)	
	Positive, %	Relevant, %	Positive, %	Relevant, %	Positive, %	Relevant, %
Methyldibromoglutaronitrile/phenoxyethanol, 2% pet	0	0	0.8	0	6.2	4.3
Tixocortal-21-pivalate, 1% pet	0	0	0.8	0.8	2.9	2.7
Cinnamic aldehyde, 1% pet[c]	0	0	0.5	0.5	2.4	1.9
Cocamide diethanolamine, 0.5% pet	0	0	0.5	0	1.2	1.0
Sesquiterpene lactone mix, 0.1% pet	7.7	0	0.5	0.3	0.6	0.5
Imidazolidinyl urea, 2% aq	0	0	0.5	0.5	1.7	1.6
Black rubber mix, 0.6% pet	0	0	0.5	0.3	1.0	0.6
1,3-Dimethylol-5,5-dimethyl hydantoin, 1% pet	0	0	0.5	0.5	2.6	2.5
Prilocaine, 2.5% pet[b]	0	0	0.5	0.5	0.1	0.0
di-Alpha tocopherol acetate, 100%[b]	0	0	0.5	0	0.5	0.4
Lidocaine, 15% pet	0	0	0.3	0.3	0.7	0.3
Dibucaine, 2.5% pet	0	0	0.3	0.3	1.0	0.4
Glyceryl thioglycolate, 1% pet	0	0	0.3	0	1.6	1.0
Hydrocortisone-17-butyrate, 1% pet	0	0	0.3	0.3	0.5	0.4
Ethyl acrylate, 0.1% pet	0	0	0.3	0	1.2	1.0
Epoxy resin, 1% pet	0	0	0.3	0	2.1	1.5
Benzocaine, 5% pet	0	0	0	0	1.8	0.9
Paraben mix, 12% pet	0	0	0	0	0.9	0.8
Methyldibromoglutaronitrile, 0.4% pet[b]	0	0	0	0	2.9	2.0
Benzophenone-3, 3% pet	0	0	0	0	0.6	0.5
Chloroxylenol, 1% pet	0	0	0	0	0.7	0.5
Methyl methacrylate, 2% pet	0	0	0	0	1.6	1.3
Phenoxyethanol, 1% pet[b]	0	0	0	0	0.2	0.2
Dimethylol dihydroxyethylene urea, 4.5% aq	0	0	0	0	1.0	0.6
Glutaral, 1% pet	0	0	0	0	1.3	0.8
Bisphenol F, 1% pet[c]	0	0	0	0	0.1	0.1
Triamcinolone acetonide, 1% pet[c]	0	0	0	0	0.3	0.3

Abbreviations: Aq, aqueous; pet, petrolatum.
[a] Overall percentage of relevance is based on the number of positive reactions to an allergen deemed of current or past clinical relevance divided by the total number tested for a specific allergen.
[b] This allergen was tested only during the 2001-2002 data cycle.
[c] This allergen was tested only during the 2003-2004 data cycle.

nosis codes listed as atopic dermatitis after the conclusion of patch testing were not more likely to have an RPPT than children without this as a final diagnosis.

IRRITANT PATCH TEST REACTIONS

The frequency of irritant patch test reactions for all allergens was greater in the adult population (n=804 [8.3%]) vs the pediatric population (n=20 [5.1%]) ($P<.03$). However, there was no statistically significant difference in the frequency of irritant reactions for individual allergens in the pediatric vs adult groups. The allergens most frequently interpreted in children as causing irritant patch test reactions included benzalkonium chloride (1.53%), cobalt (1.29%), cocamidopropyl betaine (0.52%), and nickel sulfate (0.51%). Other recorded irritant patch test reactions were noted for the following: formaldehyde, *p*-tert-butylphenol formaldehyde resin, balsam of Peru, fragrance mix, propylene glycol, tosylamide formaldehyde resin, lidocaine, dibucaine, and dimethylol dihydroxyethylene urea.

Table 5. Comparison of Top 10 Allergens With Positive Reactions and Top 10 Allergens With Relevant Positive Reactions in Children

Most Frequent Positive Reactions		Most Frequent Positive Relevant Reactions	
Allergen	No. (%)[a,b]	Allergen	No. (%)[a,c]
Nickel sulfate	111 (28.3)	Nickel	102 (26.0)
Cobalt chloride	70 (17.8)	Cobalt	48 (12.4)
Thimerosal	60 (15.4)	Neomycin	17 (4.4)
Neomycin	31 (8.0)	Fragrance mix	16 (4.1)
Gold sodium thiosulfate	30 (7.8)	Gold	14 (3.6)
Fragrance mix	20 (5.1)	Quaternium 15	14 (3.6)
Balsam of Peru	15 (3.9)	Propylene glycol	12 (3.1)
Quaternium 15	14 (3.6)	Colophony	11 (2.8)
Lanolin	14 (3.6)	Lanolin	11 (2.8)
Potassium dichromate	14 (3.6)	Bacitracin	10 (2.6)

[a] Indicates number with positive patch test reaction.
[b] Indicates percentage with a positive reaction calculated by the number of positive reactions divided by the number undergoing testing for a given allergen.
[c] Overall percentage of relevance is based on the number of positive to an allergen deemed of current or past clinical relevance divided by the total number undergoing testing for a specific allergen.

SUPPLEMENTAL NON-NACDG–RELEVANT ALLERGENS

Fifty-nine children (15.1%) had at least 1 positive reaction to a relevant non-NACDG allergen. Of all children undergoing testing, 17 (4.3%) had their only positive reaction identified by a non-NACDG supplemental allergen. **Table 6** shows sources of other non-NACDG series supplemental allergens recorded as relevant allergens.

Table 6. Source of Allergens for 59 Children With Relevant Positive (non-NACDG) Supplementary Allergens[a]

Source	Patients, %
Unknown or not applicable	14.3
Jewelry	8.6
Shoes, boots, sandals, slippers	5.7
Safety equipment, miscellaneous (eg, masks, respirators)	5.7
Recreational and athletic equipment	5.7
Sunscreens	4.3
Shirts, pants, blouses, dresses, skirts	4.3
Lipsticks	4.3
Poison ivy, oak, and other toxicodendron genus	4.3
Hair dyes	2.9
Antifungal topical medications	2.9
Cosmetics, beauty preparations, and skin and health care products	2.9
Deodorants and antiperspirants	2.9
Moisturizers, lotions, and creams	2.9
Tapes, adhesive bandage, and adhesive aids	2.9
Clothing	2.9
Inks	1.4
Writing, drawing, and art supplies	1.4
Mites	1.4
Flowers	1.4
Food products, fresh or processed	1.4
Ores, nonradiating (minerals, metallic)	1.4
Soaps and detergents, miscellaneous	1.4
Medications, topical	1.4
Hair care products	1.4
Shampoos	1.4
Nail polish	1.4
Cosmetics	1.4
Tattoos	1.4
Disinfectants (eg, alcohol, povidone iodine)	1.4
Clothing, wearing apparel, protective equipment, textiles	1.4
Watches	1.4

Abbreviation: NACDG, North American Contact Dermatitis Group.
[a] Indicates 15.1% of all children undergoing testing. Only 1 supplemental allergen could be reported.

COMPARISON WITH T.R.U.E. TEST PANELS 1.1 AND 2.1

The hypothetical ability of currently available allergens or allergen mixes on T.R.U.E. TEST panels 1.1 and 2.1 was compared with allergens with positive relevant reactions found in children by the NACDG series. Of the 200 children with RPPTs, 123 (61.5%) would have had all their relevant positive reactions to allergens detected by the T.R.U.E. TEST if only the T.R.U.E. TEST had been used. Neither test series would have detected the supplementary positive allergen reactions reported in 15.9% of children.

COMMENT

To our knowledge, this is the first multicenter study to evaluate the frequency of reactions to contact allergens in North American children referred for patch testing. Nickel (28.3%), cobalt (17.8%), thimerosal (15.4%), neomycin (8.0%), gold (7.8%), and fragrance mix (5.1%) were the allergens with the most common positive reactions on patch tests in this pediatric population. Of these, neomycin and gold are allergens that differ on our list of allergens with the most frequently positive reactions compared with previous international studies, likely reflecting geographic differences in the patterns of use and testing. For instance, neomycin use is less common in Europe and Asia than in the United States. Although most patch tests with positive reactions to nickel also are considered to have current or past relevance, less than half of those with positive reactions to gold in our study were deemed relevant, and none of the 3 positive reactions to gold in children younger than 5 years were deemed relevant.

The most relevant allergens in children—nickel, cobalt, neomycin, fragrance mix, and lanolin—are expected, given the probable use and exposure patterns to these allergens in children. Our focus on relevance has identified the importance of additional allergens in children, including quaternium 15, propylene glycol, colophony, and bacitracin. According to our study, 3 other allergens commonly yield positive reactions but often are less clinically relevant, including thimerosal, *M pereirae* (balsam of Peru), and potassium dichromate.

Our study showed significant differences between the frequency of individual positive reactions to allergen patch tests in children and adults; children were more likely to have reactions to nickel, cobalt, thimerosal, and lanolin, whereas adults were more likely to have positive reactions to neomycin, fragrance mix, *M pereirae* (balsam of Peru), and quaternium 15.

Differences in the frequency of positive reactions to patch tests for a given allergen among different age groups likely reflect differences in the age at exposure and the frequency, type, and length of exposure required to induce sensitization to specific chemicals. For example, nickel exposure likely occurs earlier in life, is frequent, and could require less exposure to create sensitization, whereas neomycin exposure may be the opposite.[11] Buckley et al[12] found that in a UK population, positive patch tests to fragrance were infrequent in the first few decades of life and increased gradually after 20 years of age to peak in the seventh decade of life in women and eighth decade of life in men. They hypothesized that fragrance sensitivity results from repeated environmental exposure and age-related susceptibility factors. This may help explain why 4.1% of children in our study undergoing testing to fragrance mix had a positive, relevant patch test reaction compared with 8.7% in the adult group.

As in our study, nickel was the most common allergen in children in 14 of the 17 studies of patch testing summarized by Mortz and Andersen[1] and in 5 of 7 more recent studies summarized in Table 1. Our group found 28.3% of children had positive reactions to nickel; most of these had current or past relevance. In contrast to our study, Clayton et al[3] in the United Kingdom reported that 33% of children had positive reactions to nickel, although only 3 cases were deemed of current relevance. Nickel was the most common allergen with positive reactions in the study by Roul et al,[8] but positive reactions did not often correlate with exposure. In contrast to nickel, patch tests with positive reactions for thimerosal (15.4%) are more often of little to no current or past relevance in our population. The development of an allergy to thimerosal is likely a result of routine vaccination. At pres-

ent, however, thimerosal is infrequently used in topical products, which likely accounts for the limited relevance of a positive patch test reaction in North American children. For this reason, thimerosal was removed from the 2003-2004 NACDG screening allergen series.

Two recent publications provide patch test results on asymptomatic pediatric populations. Data from 1501 eighth grade school children in Denmark showed 15.2% of children had at least 1 positive allergen reaction, and 47.7% of these were suspected to be relevant to past dermatitis. Nickel and fragrance were deemed the most frequent relevant allergens.[13] A US population-based study of 95 healthy asymptomatic children aged 6 to 67.5 months showed the prevalence of sensitization was 24.5% (≥1 positive reaction to an allergen); no measure of relevance was given.[11] Bruckner et al[11] point out that age of sensitization can occur very early; 45% of patients with positive reactions were younger than 18 months. The top 5 allergens in this asymptomatic population undergoing screening were nickel (12.9%), thimerosal (9.4%), methylchloroisothiazolinone/methylisothiazolinone (2.4%), neomycin (1.2%), cobalt (1.2%), and *p-tert* butylphenol (1.2%). Seven of the 11 reactions to nickel occurred in children younger than 16.5 months, a finding supporting that the age of sensitization for some allergens is quite early in life. The source of nickel was reported as jewelry and fasteners.[11] Our data on early sensitization and positive patch test reactions in children younger than 5 years are included in Table 4 for comparison. Children aged 0 to 5 years had relevant positive reactions to nickel, cobalt, neomycin, quaternium 15, bacitracin, tea tree oil, and iodopropynyl butylcarbamate (a preservative). Tea tree oil sensitization in this young group implicates likely use and exposure and suggests parental interest in using natural products that probably are perceived as being safer. Sensitization can and does occur early in life. Sensitization, however, does not necessarily equate with clinical disease.

Prior studies have suggested that children with atopic dermatitis are less or equally likely to have contact dermatitis.[14] In our population, children with a history of atopic eczema were equally likely to have RPPTs than children without such history. Of those with an RPPT, children (34.0%) were more likely than adults (11.2%) to have a final diagnosis that included atopic eczema. These data suggest that atopic eczema is a more important risk factor for ACD in children than adults. However, this could reflect recall bias, because atopic eczema is more common in children, and/or referral bias, because children with a history of eczema represented 40.2% of the pediatric group compared with 17.2% of adults.

Rietschel and Rosenthal[15] investigated irritant patch test reactions using retrospective results of testing with a standard NACDG allergen series from 1984 to 1987. They reported 11% irritant reactions in the group 80 years or older, 9% in the group aged 20 to 64 years, and no irritant reactions in the group aged 0 to 12 years. Modification of allergen concentrations for patch testing in the young or the elderly group was deemed unnecessary, in concordance with other studies on this topic.[11,16,17] Our results on irritant patch test reactions in children supports this conclusion.

Strengths of this study include the fact that it was multicentered, a large number of children underwent testing, and the relevance of the patch test results was determined. Although relevance data were determined after patch testing and in most instances, not after lengthy follow-up, they serve as an estimate of the usefulness of a positive patch test reaction. An RPPT ideally should result in avoidance of the allergen and improvement or cure of the problem. Relevance is best determined by follow-up over time, but this type of follow-up study is costly and time intensive.

These data are mainly useful as a guide to the selection of allergens used for patch testing in children in North America. The allergen hit list outlined by Wöhrl et al,[6] the allergens with a positive yield outlined by Beattie et al,[2] the most frequent allergens in children identified by Clayton et al,[3] and a shortened standard series for children outlined by Roul et al[8] provide similar guidance for screening allergens with the highest yield for patch testing children in particular locales.

Our findings also confirm the role for more expanded allergen testing in children who fail to improve after T.R.U.E. TEST screening and avoidance of those allergens with positive reactions. The top 44 most frequently positive relevant allergens (minus the low-relevance allergens benzalkonium chloride and thimerosal) would pick up 95% of relevant positive reactions in children tested with the broader NACDG screening series. Patch testing should be considered for children with persistent eczema, difficult-to-control or worsening atopic eczema, or a distribution of eczematous dermatitis suggestive of allergic contact allergy.

These results may not be generalizable to all children undergoing patch testing. Children referred to an NACDG member for patch testing are selected subsets; these children are more likely to have more severe and/or more chronic dermatitis and to have been referred by a dermatologist. Relatively few black, Hispanic, or Asian children are represented. Another limitation is the difficulty, if not impossibility, of determining whether a weak reaction truly represents allergy, or if such reactions represent false-positive, irritant reactions. We did not evaluate the strength (mild, moderate, or severe) of positive reactions, although relevance partially addresses this concern.

CONCLUSIONS

Patch testing in children suspected of having ACD is a valuable endeavor. Despite their limited back size, an expanded allergen series helps to identify important positive relevant allergens. Allergen concentration does not need modification for testing in children. Of the children suspected of having ACD and referred to a specialized center for testing, 51% had at least 1 positive patch test result considered relevant. Relevant positive reactions to the patch tests were equally frequent in children and adults, although the most frequent relevant allergens differed. Nickel, cobalt, neomycin, fragrance, gold, quaternium 15, propylene glycol, colophony, lanolin, and bacitracin were the most common RPPT allergens in North American children suspected of having ACD. The top 45

allergens with the most frequent positive and relevant reactions reported in this study should serve as a guide to patch testing in children suspected of having ACD in North America. Including supplemental allergens to the patch test materials based on clinical suspicion is also useful in some patients.

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